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# UNIVERSITY of PENNSYLVANIA

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## *The School of Medicine*

THE ELDRIDGE REEVES JOHNSON  
FOUNDATION FOR MEDICAL PHYSICS

October 28, 1960

Please Address Reply to:  
612 Maloney Building

Dr. Joshua Lederberg  
Department of Genetics  
Stanford University  
Palo Alto, California

Dear Joshua:

Thank you for your letter and for a reprint of your extremely stimulating article on Exobiology. I have thought very much about this article and certainly believe that it is an appropriate one for consideration at the present time. I suppose that I did speculate a little bit on the temperature problem recently in view of the rather surprising light-induced cytochrome oxidation we obtained for the intact photosynthetic bacteria at liquid nitrogen temperatures.

Your block diagram nicely indicates the nature of the problem. It is appropriate to emphasize at the beginning that the speed with which the detector can operate depends entirely upon the amount of material which can be concentrated by the collector system. If the material can be obtained in high concentration, then, indeed a rapid scanning device will operate satisfactorily. If, however, a single cell is to be detected, a sufficient time for an accurate measurement must be allowed. My own activities involve microspectrophotometry and microfluorimetry, for the identification and localization of metabolically active components of the cell as distinguished from those involved in longer term processes such as nucleic acid or proteins in general.

I enclose a couple of papers which describe two methods, one spectrophotometric, the other fluorometric which seem to be equal in their sensitivity, namely, 6,000 - 10,000 molecules of cytochrome or pyridine nucleotide respectively.

The limitations are formidable. Our methods will not work on very small cells, optimal size now appears to be 3 to 6 micron body such as a mitochondrial aggregate or nebenkern. The registration time is long, a few seconds are required for the measurement, of the component in one form (oxidized or reduced) but it is highly desirable to see whether it can be changed into another form by a suitable shift in the metabolic environment.

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In order to increase the sensitivity one would have to use brighter but non-destructive light and more sensitive phototubes with somewhat better aperture optics. Perhaps a greater degree of sophistication in the circuitry would be necessary. These problems really impinge upon our store of knowledge in the Physics and Chemistry of light sources and photo-sources. It seems to me that this is the point at which a considerable investment is worthwhile.

There are a number of people working on uv scanning methods. In fact, I note that a symposium will be organized around these techniques. Exclusive of such people working on low sensitivity uv scanners, only a few persons are capable of carrying on component developments. There is, of course, the Zurorykin group at the Rockefeller consisting mainly of Carl Berkeley and one or two others. This group is not of the highest standard. Walter Tolles at Airbourne Instrument Laboratory in Long Island has been working in the general area for some time and may be pretty good at it. I will give a lecture on microspectrophotometry and microfluorometry to the Long Island Section of the IRE next week and if I find out anything earth-shaking will let you know. There is a group at Camp Dietrich which has been using infrared but has a peripheral interest in ultraviolet. Two groups are doing fluorometry of cell preparations. One of them is Rodney Olson at NIH, the other one is a fellow named Loesser who I believe is at Western Reserve. Abroad, there is Cuspersson's group which has made no significant technical contributions for a number of years, however, one of his students, Bo Thorell, and his engineer Lenny Akerman have been working in the closest collaboration with us and I think are fairly well qualified. There are probably many other groups with which I am not familiar. However, this list together with the enclosed collection of papers should give you a good thought on the problems that you mentioned.

Will we see you here at the Academy Meetings?

With best regards to all,

Very sincerely yours,



Britton Chance

BC:sb

Enc.

*New York Acad Sci Oct 1961.*